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OPINION

Multidimensional assessment and tailored interventions for COPD: respiratory utopia or common sense?

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ABSTRACT

Introduction The rising disease burden from chronic obstructive pulmonary disease (COPD) requires new approaches.

Method We suggest an approach based around three elements: inflammometry and multidimensional assessment to identify therapeutic targets and case management to design and implement an individualised treatment programme based on these assessments.

Discussion This tailored approach to treatment would maximise efficacy, limit cost and permit a better risk–benefit ratio of treatment. The advantages include the ability to add up the benefits of individual therapies leading to a cumulative therapeutic benefit that is greater than each individual therapy alone. We can now design a multifaceted inflammometry intervention for airway diseases based on targeting eosinophilic inflammation, non-eosinophilic pathways and systemic inflammation. COPD is a complex and challenging disease. The use of inflammometry and multidimensional assessment is necessary to identify relevant treatment targets and maximise the scope of therapy while limiting unnecessary use of drugs. An individualised programme of management can be designed and coordinated by using a case manager. This new approach may provide tangible benefits to people with COPD.

Chronic obstructive pulmonary disease (COPD) is a high impact disease,¹ with a global trajectory that predicts an alarming increase in illness burden.² Current approaches are unlikely to be sufficient to address this problem since they are largely based around disease management concepts that have been available for several years, at a time when the global COPD burden is escalating. New approaches are required and we suggest an approach that is based around three elements: the use of *inflammometry* and *multidimensional assessment* to identify therapeutic targets, and *case management* to design and implement an individualised treatment programme based on these assessments.³ Some see this as self-evident (common sense), whereas others see it as idealistic (respiratory utopia). We maintain it is both of these things, and more, since it offers a pragmatic and achievable approach to a complex condition, with the prospect of major health gains.

At the core of this approach is recognition of the heterogeneity in COPD. There is now considerable editorial space devoted to this subject.^{3–6} But do we actually apply this knowledge to the management of COPD?

Improvement in health status and avoidance of exacerbations are the key goals of management⁷ and it is now time to consider the heterogeneity of this disease in terms of treatment approaches. The current method is to apply a blanket approach to pharmaco-therapy that is informed by disease severity. The recently revised Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy suggests a graded approach to managing COPD, which involves short-acting bronchodilators and active reduction of risk factors (smoking cessation and vaccinations) across all COPD severity classifications.⁷ Pharmacotherapies including inhaled corticosteroids, long acting β agonists (LABAs), long-acting antimuscarinics (LAMAs), theophylline and phosphodiesterase-4 inhibitors (PDE4) are recommended as severity, exacerbation frequency and symptoms increase.⁷ Newer therapeutic choices that target the inflammatory processes in COPD show great promise and their evidence base is increasing. These agents include macrolides as antibiotic/immunomodulatory agents^{8–10} and 3-hydroxy-3-methyl coenzyme A reductase inhibitors (statins) for systemic inflammation.¹¹ However, because of the heterogeneity of COPD, the positioning of these agents in COPD pharmacotherapy is unclear. The currently recommended anti-inflammatory treatment (inhaled corticosteroid) does not improve systemic inflammation,¹² may worsen neutrophilic airway inflammation¹³ and when applied generally in COPD has a worrying pneumonia risk.¹⁴ Recent and ongoing studies (<http://www.clinicaltrials.gov>) of anti-inflammatories in COPD apply single agents generally to all patients with COPD. This approach fails to recognise the heterogeneity of inflammation in this disease and results in a therapeutic paradox, when key pathophysiological processes can escape therapeutic intervention.

This raises the question of whether a tailored approach to treatment would maximise efficacy, limit cost and permit a better risk–benefit ratio. With this approach the benefits of individual therapies are each added together to bring a cumulative therapeutic benefit. Such multifactorial intervention is common with non-pharmacological therapies, such as pulmonary rehabilitation and asthma self-management education. Together with multidimensional assessment, it is also used successfully in other chronic diseases. The core elements of this approach are inflammometry (table 1), multidimensional assessment³ and case management. This

Table 1 Inflammation-based algorithm

Component	Management
Airway inflammation	
Eosinophilic (sputum eosinophil count %>3)	ICS 500 µg twice daily (beclomethasone equivalent) and prednisolone according to Siva ²³
Neutrophilic (sputum neutrophil count %>61)	Azithromycin 250 mg daily for 3 months
Mucus hypersecretion	Positive expiratory pressure device (Acapella) Hypertonic saline 6% twice daily, nebulised
Systemic inflammation (CRP >3 mg/litre)	Simvastatin 20 mg daily for 3 months
If systemic inflammation and neutrophilic airway inflammation were present doxycycline was used in place of azithromycin to avoid coadministration of simvastatin and azithromycin. CRP, C-reactive protein; ICS, inhaled corticosteroid.	

article reports the concept, design and pilot testing of this approach.

REAL WORLD EXAMPLE OF AIRWAY INFLAMMOMETRY CASE MANAGEMENT

Older adults (>55 years) with stable COPD (defined in online supplement) were recruited and allocated to usual care (n=19) or multidimensional assessment and management (n=17). The intervention consisted of individualised management based on the baseline multidimensional assessment. A personalised care plan was developed by the study physician and case manager. The clinicians and participants agreed on the tailored interventions for each of the identified problems.¹⁵ An inflammation algorithm (table 1) was used to inform treatment decisions for airway inflammation, systemic inflammation and mucus hypersecretion. Other tailored interventions were standardised according to the best available evidence.³ The case manager coordinated the plan. The interventions were delivered over 3 months during individualised visits (see online supplement table 1). Pulmonary rehabilitation participation occurred concurrently.

The participant characteristics are presented in table 2. The baseline multidimensional assessment identified a mean (95% CI) of 10.5 (9.7 to 11.2) clinical management problems per participant. These problems clustered into four domains: airway related problems, comorbidity, risk factors and behavioural issues.³

The primary outcome of health status improved significantly from baseline to 3-month follow-up in the intervention group. The mean (95% CI) difference in St George's Respiratory

Questionnaire (SGRQ) for multidimensional assessment, airway inflammation and individualised management (MDAIM) was 14 (20.7 to 8.5) versus 3.5 (-3.8 to 10.8); p=0.0003 for control (figure 1A). The mean (95% CI) SGRQ score post intervention for MDAIM was 42.8 (35.3 to 50.4) versus 52 (45.1 to 58.9); p=0.06 for control.

Clinically significant quality of life improvement (decreased SGRQ score > 4 units at 3 months) was achieved in 14 (82.3%) participants in the MDAIM group and 5 (31.2%) in the control group (p=0.003). The number needed to treat in order for one person to achieve a clinically significant change in SGRQ was 2.

In the MDAIM group health status continued to improve at 6-months follow-up (mean (95% CI) decrease of 17.1 (7.1 to 27.1) units, p=0.002) and was maintained at 12 months with a 13.5 (4.7 to 22.3) unit decrease from baseline (p=0.005). In the control group there was no statistically significant difference at either 6 months (4.5 (-1.2 to 10.3); p=0.1) or 12 months (3.1 (-3.5 to 9.7); p=0.3).

Targeted inflammation-based management reduced eosinophilic and neutrophilic airway inflammation and systemic inflammation (figure 1B–D).

DISCUSSION

Airway and systemic inflammation in COPD is heterogeneous and since any one person can exhibit more than one inflammatory process (figure 2), any individual may require more than one therapeutic approach. For example, targeting neutrophilic inflammation alone will treat 57% of people with COPD (figure 2).¹⁶ Targeting eosinophilic inflammation will treat a further 34% and

Table 2 Baseline participant characteristics

	Intervention	Control
N	17	19
Gender, M F	5 12	13 6
Age (years), mean (95% CI)	70.6 (65.8 to 75.4)	71.1 (67.1 to 75.2)
Post-bronchodilator FEV1% predicted, mean (95% CI)	55 (43.5 to 67.2)	48 (40.2 to 55.3)
Post-bronchodilator FVC % predicted, mean (95% CI)	71 (63.1 to 79.2)	67 (59.3 to 73.6)
FER, mean (95% CI)	0.59 (50.8 to 67.2)	0.51 (50.8 to 67.2)
SGRQ (units), mean (95% CI)	57 (51.5 to 63.4)	50 (44.0 to 55.5)
Smoking status, never ex current	0 15 2	0 15 4
Charlson comorbidity index, mean (95% CI)	4 (3.3 to 4.7)	4.1 (3.7 to 4.5)
BMI (kg/m ²), mean (95% CI)	27.8 (24.1 to 31.5)	28.4 (24.6 to 32.4)
CRP (mg/litre), median (IQR)	5.3 (2.5–9.5)	6 (2–9)
Sputum neutrophils (%), mean (95% CI)	59 (43.3 to 74.7)	59 (46.5 to 71.9)
Sputum eosinophils (%), median (IQR)	2.25 (1–7)	1.75 (0.5–2.65)

BMI, body mass index; CRP, C-reactive protein; FER, forced expiratory ratio; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; SGRQ, St George's Respiratory Questionnaire.

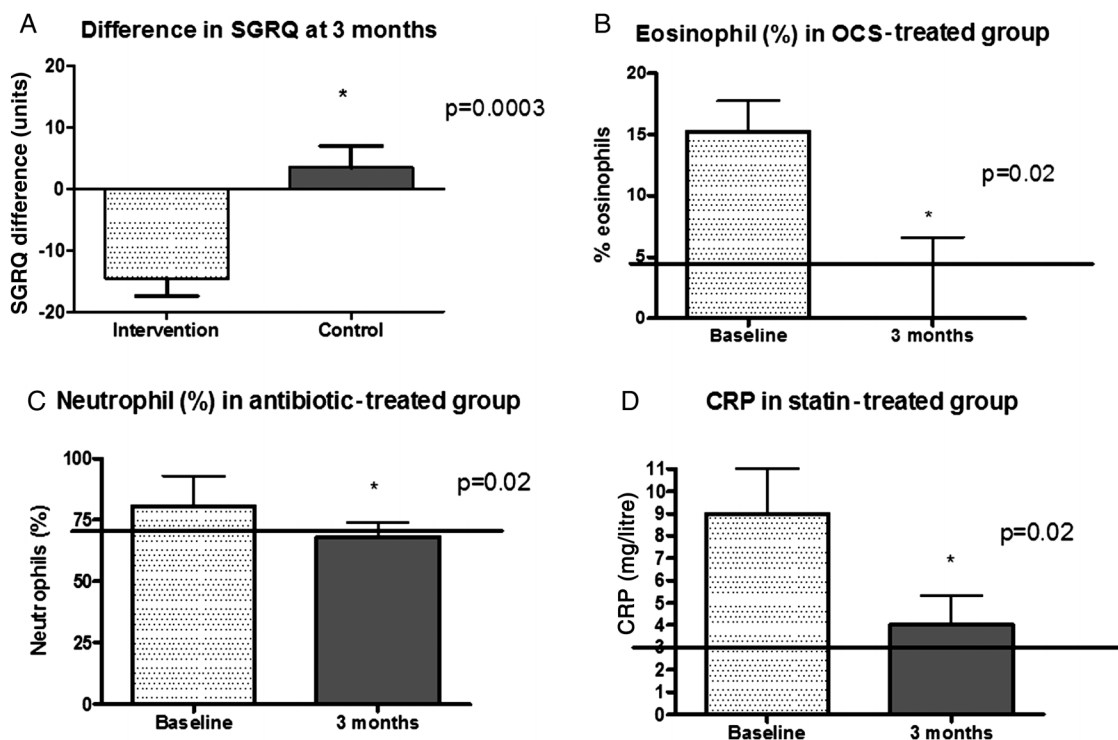


Figure 1 Biomarkers of inflammation in the group receiving treatment tailored to inflammation using the inflammation treatment algorithm. (A) Health status measured by St George's Respiratory Questionnaire (SGRQ) improved significantly (lower score) in the intervention group and worsened in the control group, as measured at 3 months. (B) In the group within multidimensional assessment, airway inflammometry and individualised management (MDAIM) that received oral corticosteroids (OCS) sputum eosinophils (%) had normalised post intervention. The solid line represents the upper limit of normal for sputum eosinophils. (C) In the group within MDAIM that received antibiotics as anti-inflammatory agents sputum neutrophils (%) had normalised post intervention. The solid line represents the upper limit of normal for sputum neutrophils. (D) In the group within MDAIM that received statins for systemic inflammation there was a statically significant reduction in serum high-sensitivity C-reactive protein (hs-CRP). The solid line represents the upper limit of normal of hs-CRP.

targeting systemic inflammation will manage this problem in 59% of the COPD group. Drug therapy is increasingly pathway specific, and to target all of these different pathways in all people with COPD would require three drugs, that is, macrolide, statin and corticosteroid. A less costly and potentially safer approach is to use individual assessment and multicomponent therapy. We have

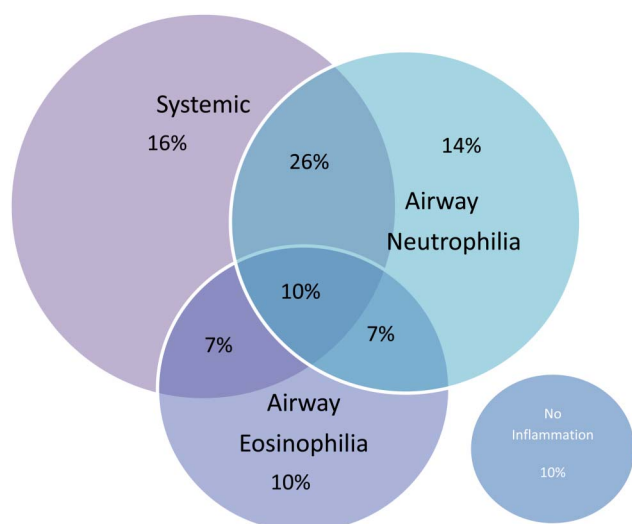


Figure 2 Venn diagram showing the prevalence of different inflammatory processes in chronic obstructive pulmonary disease. This figure is only reproduced in colour in the online version.

developed a multifaceted approach that is likely to be highly effective and may be safer.^{3 17} The additive effects of targeted anti-inflammatory treatment to eosinophilic, neutrophilic and systemic inflammation should show at least cumulative benefits, and result in a greater proportion of the COPD population receiving effective anti-inflammatory therapy. We recognise that anti-inflammatory treatment in COPD needs to balance the nature of inflammation, treatment efficacy and the potential for adverse effects. For example, the broad application of macrolides is effective⁸ but there is a concern about side effects and microbial resistance. Consequently, an individually targeted approach may be a better way to maximise efficacy and minimise side effects.

Inflammometry

Current evidence can now be used to design a multifaceted inflammometry intervention for airway diseases. High-quality evidence reports the superior effects of targeting airway eosinophilic inflammation in asthma and COPD,^{9 18–23} with a 50% reduction in exacerbations. Non-eosinophilic inflammatory pathways are addressed using macrolide antibiotics as immunomodulatory agents and studies demonstrate reductions in exacerbations, improved lung function and improved health status.^{8 9} Systemic inflammation represents a further pathway that could be identified by inflammometry and targeted by statins. In COPD an increasing number of observational studies report the positive effects of statins, including a reduced number of COPD exacerbations,^{24–26} reduced lung function decline,²⁵ improved exercise capacity²⁷ and reduced mortality.^{11 26 28 29} These

published studies have targeted specific inflammatory processes in isolation, and while they show efficacy, to date there are no other published studies other than these pilot data that treat the overlapping features of the inflammatory processes present in individuals with COPD. Our composite inflammatory algorithm is described (table 1).

Case management

The needs of patients with COPD are complex and multidimensional, and as clinicians, our responses must also be multidimensional and integrated to meet these needs. Case management is an approach that offers a solution to these healthcare delivery issues in COPD. This approach can be used to complement individualised and phenotype-based treatments in this complex population.

This approach brings together multidimensional assessment, inflammometry and case management. It need not be restricted to COPD, but could usefully be applied to other chronic airway diseases, such as severe asthma and bronchiectasis. We have targeted problems that clustered into four domains: airway-related problems, comorbidity, risk factors and behavioural issues. There are additional issues that could be addressed and require further consideration, such as end of life care and whether disease severity using either GOLD stage or BODE (body mass index/airflow obstruction/dyspnea/exercise capacity) index has an impact on problem assessment and management.

When looking at the prospects and challenges of COPD management in the future, this form of respiratory utopia makes a certain amount of commonsense!

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Contributors VMCD: project conception, study design, data collection, data analysis, data interpretation, writing and revisions of the manuscript, study design and revisions of the manuscript. IH: study design and review of manuscript. LGW: study design and review of manuscript. PGG: project conception, study design, data interpretation, and writing/revision of manuscript.

Competing interests Dr Vanessa McDonald has been reimbursed for participation in educational meetings from AstraZeneca, Boehringer Ingelheim GlaxoSmithKline and Novartis. She has participated in studies funded by GlaxoSmithKline. Professor Isabel Higgins has no competing interests to declare. Dr Lisa G Wood has no competing interests to declare. Professor Peter Gibson holds an NHMRC Practitioner Fellowship. He has been reimbursed for participation in symposia funded by AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline and Novartis. He has participated in studies funded by Pharmaxis and GlaxoSmithKline.

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Multidimensional assessment and tailored interventions for COPD: Respiratory utopia or common sense?

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Methods:

The inclusion criteria were: age ≥ 55 years and stable asthma and or COPD, with airflow obstruction defined by a pre-bronchodilator forced expiratory ratio (FER) < 0.7 and Forced Expiratory Volume in 1 second (FEV_1) $< 80\%$ predicted. Ability to attend study visits and satisfactory English language skills were needed. Exclusion criteria included: significant co-morbidities that the study may have impacted on, or an anticipated life expectancy of < 3 months.

The study was conducted according to the International Conference on Harmonisation Good Clinical Practice Guidelines and was approved by the Hunter New England Ethics committee. The ACTRN registration number is 12611001278921.

Treatment allocation

Participants were allocated to either the MDAIM intervention or usual care control groups, using pre-determined criteria (the postcode of the participants' residential address) and allocation was concealed from the referring and treating doctor.

Study Design

All eligible participants underwent a previously developed and tested single visit multidimensional assessment to measure clinical, functional, biological and psychosocial outcomes (Table 1). [1, 2] This assessment focused on the components of airway disease, co-morbidity, COPD self-management skills and risk factors (Table 1).

The intervention group participants were rescheduled for the following week, reviewed by the case manager and dietician and the care planning exercise was conducted. Subsequent visits were scheduled according to the treatment plan (table 1). The control group had their physician and pulmonary rehabilitation (PR) visits scheduled by their usual care treating team.

Participants were followed up at 3, 6 and 12 months for repeat multidimensional assessment. If the control participants had not yet completed their pulmonary rehabilitation programme (PRP) at 3

months, the study follow-up visit was postponed for a maximum of 4 weeks to enable completion of this aspect of usual care.

Participant flow

Thirty-six participants were recruited to the study and were randomised to the intervention (n=17) or the control (n=19) group (Figure 1). All participants in the intervention group and 17 in the control group completed the 3 month follow-up. There were 4 participants in MDAIM who experienced 5 adverse events that were secondary to the intervention treatment. Over 12 months there was 1 death in the MDAIM group and 2 in the control group. The cause of death in the intervention participant was cardiovascular disease, in the control group one participant died of respiratory failure and the other of renal failure.

Intervention

MDAIM

The intervention consisted of individualised management based on the baseline multidimensional assessment. A personalised care plan was developed by the study physician and case manager. The clinicians and participants agreed on the tailored interventions for each of the identified problems[3]. An inflammometry algorithm (Table 1 manuscript) was used to inform treatment decisions for airway inflammation, systemic inflammation, and mucus hypersecretion. Other tailored interventions were standardised according to best available evidence (Table 1).[1] The case manager coordinated the plan. The interventions were delivered over 3 months during individualised visits. PRP participation occurred concurrently.

Control

The control group received medical assessment, pharmacotherapy and ongoing management by a respiratory physician and referral to a PRP.

Procedures

QOL was assessed using the Saint George Respiratory questionnaire (SGRQ).[4] Airflow obstruction was assessed by spirometry (KoKo K313100 PDS Instrumentation, Louisville, CO, USA) to measure pre and post-bronchodilator FEV₁, FVC and FER according to ATS/ERS standards.[5] Predicted FEV₁ and FVC were calculated using NHANES III.[6]

Airway inflammation was assessed using induced sputum.[7] Lower respiratory sputum portions were selected from saliva, processed using dithiothreitol and differential cell counts obtained.[8]

Peripheral blood was collected for assessment of systemic inflammation, using high sensitivity C Reactive Protein (hs-CRP) analysed using the Siemens Healthcare Diagnostics (Marburg, Germany) ELISA. The analytical measurement range for this kit was 2.90 – 190mg/L.

Mucus hypersecretion was assessed using six items from the 1978 ATS/DLD Respiratory Symptom Questionnaire.[9] Participants reported on the presence, frequency, volume and colour of sputum expectorated. All other assessments are described in the online supplement and Table 1.

Analysis

Health status, measured by the SGRQ, was the primary outcome.[4] Secondary outcomes included: the number of problems detected using the multidimensional assessment, exacerbations, sputum cell counts and CRP. An intention to treat analysis was performed. All data were analysed using Stata 10 (Stata Corporation, College Station, Texas USA). Parametric results are reported as mean (CI) and non-parametric results as median (IQR). Parametric data analysis was performed using Students' paired and non-paired t-tests as appropriate and the Chi square test for categorical data. Non-parametric analyses were performed using the two-sample Wilcoxon Rank Sum, the Kruskal-Wallis test for more than two groups, and Fisher's exact test for categorical data. Poisson regression was used to analyse differences in hospitalisations between groups and the incident rate ratio (IRR) reported. Results were reported as significant when $p < 0.05$.

Results

Number of clinical management problems

The intervention led to a statistically significant decrease in the number of clinical problems. The mean (CI) number at baseline was 10.2 (9-11.4) per participant for MDAIM. This was reduced to 6.4 (5-7.7); $p = 0.0001$ after the intervention, which was also significantly fewer than the control group,

who post treatment had 10.3 (9.1-11.6) problems per participant ($p= 0.0001$). The mean change (reduction) in number of problems for the MDAIM was -3.8 (-5.3- -2.3) compared to 0.5 (-2.1-1.1); $p=0.003$ for the control group.

Lung Function

No differences were found between the groups in any of the lung function parameters.

Exacerbations

Over 12 months there were 46% (IRR=0.54; $p=0.28$) less admissions in the MDAIM group compared to control, however this did not reach statistical significance. Over 12 months there were fewer dropouts in the MDAIM; $n=3$ (17.6%) compared to control; $n=8$ (42%).

Individualised interventions received by the MDAIM group

Inflammation based management

The 5 participants with eosinophilic airway inflammation were all prescribed ICS at baseline. They received oral corticosteroids and the baseline median (IQR) sputum eosinophil % of 15.5 (7-15.7) decreased to 0 (0-4) ($p=0.02$) post intervention (Figure 1b manuscript). Sputum neutrophilia was detected in 6 (35.2%) participants. Targeted antibiotic therapy significantly improved and normalised sputum neutrophilia from a mean (CI) baseline sputum neutrophil % of 81.8 (72.1-91.5) to 55.8 (33.7-78.0) post intervention; $p=0.02$ (Figure 1c manuscript). CRP was $>3\text{mg/L}$ in 11 (64.7%) of the MDAIM participants who were treated with simvastatin for 3 months. There was a significant reduction in CRP from a median (IQR) baseline of 9 (5-11) to 4 (1-5.3) mg/L post treatment; ($p=0.02$). To aid in mucociliary clearance, 11 participants with mucus hypersecretion received a positive expiratory pressure device with education and follow-up. Of these, 6 were also treated with nebulised hypertonic saline (6%, 10mL bd). At follow-up, mucus hypersecretion was present in only 4 of the 11 participants ($p=0.04$).

Table 1: Multidimensional Assessment and Individualised Management

Clinical Problem	Assessment and guiding principle for identification	Individualised Management
Airway Components		
Exercise intolerance	6 minute walk (6MW) distance < 350 metres [10]	Pulmonary rehabilitation and home based training
Airflow obstruction	FEV ₁ /FVC ratio <70%, and FEV ₁ <80% pred	Long-acting bronchodilator therapy [Table 2]
Airway inflammation	Induced sputum: Neutrophils >61%; Eosinophils>3%; Mixed = Neutrophils >61% & Eosinophils>3% [11]	Included tailored pharmacotherapy according to inflammation based algorithm [Table 2]
Frequent chest infections	≥ 2 antibiotic courses in 12 months for lower respiratory tract infections	Written action plan with antibiotic choice tailored to baseline sputum pathogens
Pathogen Colonisation	Sputum culture positive for a recognised bacterial pathogen	Written action plan with antibiotic choice tailored to baseline sputum pathogens
Mucus hypersecretion	A volume ≥ 25mls of mucus produced daily for the last week in the absence of an infection	Tailored therapy according to inflammation based algorithm[Table 2]
Oxygen desaturation	SpO ₂ < 90% either at rest or during 6MW test	Investigation and implementation of domiciliary oxygen therapy and nasal CPAP
Co-morbidity		
Assessment tools	Defined as all comorbid medical conditions, that were current and significant.	Guideline based management
Anaemia	Haemoglobin <120g/L Female or <140g/L Male	Guideline based management
Anxiety Depression	Hospital Anxiety and Depression Scale (HADS) Anxiety domain score ≥8 or Depression domain score ≥ 8[12]	Counselling, Cognitive Behavioural Therapy +/- paroxetine 20mg daily
Cardiac dysfunction	NT-proBNP >1000fmol/ml; chest radiograph	Guideline based management
Dysfunctional breathing	Nijmegen questionnaire Total score ≥23[13]	Breath retraining, including pursed lip breathing, active expiration, diaphragmatic breathing, adapting specific body positions, and coordinating paced breathing with activities. Techniques were reassessed and reinforced throughout the intervention period.
Systemic inflammation	Hs-CRP >3mg/L	Tailored pharmacotherapy according to inflammation based algorithm
Obstructive Sleep Apnoea	Epworth sleepiness scale Score >8 suggests need for further investigation[14]	Investigation and implementation of domiciliary oxygen therapy and nasal CPAP
Self-management Skills		
Exacerbation management	Patient does not possess a WAP or does not use the prescribed plan during exacerbations	Written action plan and self-management education Improvement of knowledge
Inhaler device polypharmacy	Prescription of ≥ 3 different inhaler devices[15]	Minimise devices, inhaler technique education

Inhaler device technique	Technique rated as inadequate[16]	Inhaler technique skills
Non Adherence	Reported use of <80% of prescribed treatment	Correction of adherence
Risk Factors		
Smoking	Admit to smoking and exhaled CO ≥ 10 ppm or deny smoking and show exhaled carbon monoxide ≥ 10 ppm	Counselling plus Nicotine Replacement therapy or Varenicline
Malnutrition Overweight Obesity	BMI $< 20 \text{ kg/m}^2$ BMI between 27 & 30 kg/m^2 BMI $> 30 \text{ kg/m}^2$	3 pronged intervention tailored to BMI. All received an individualised dietetic intervention, delivered by an accredited practicing dietitian. Advice: the components of a balanced diet, promoting anti-inflammatory foods high in Omega 3 fatty acids, antioxidants and calcium for bone health. Underweight –Healthy intervention plus nutritional supplements and counselling. Dietetic information regarding weight gain, including a high protein (1.2-1.5g Protein per Kg Ideal Body Weight), high energy (120% of Estimated Energy Requirements) eating plan and a nutritionally complete oral supplement (Two Cal HN, Abbott Nutrition and/or Sustagen Hospital Formula, Novartis Nutrition). Overweight – Healthy intervention plus dietetic intervention that focused on weight reduction/weight maintenance through a non very low calorie diet.
Sarcopenia	DXA: Appendicular skeletal muscle mass index $< 5.45 \text{ kg/m}^2$ (female) and 7.26 kg/m^2 (males)[17]	Muscle resistance training and high protein diet
Activity limitation	Defined as self-reported impairment due to an inability to achieve personal activity goals	Pulmonary rehabilitation and home based training

6 MW – 6 Minute walk

FEV₁-Forced Expiratory Volume in 1 second

FVC -Forced Vital Capacity

CPAP- Continuous Positive Airway Pressure

SpO₂- Pulse oximeter Oxygen Saturation

HADS – Hospital Anxiety and Depression Scale

BMI – Body Mass Index

DXA –Dual energy X-Ray Absorptiometry Hs CRP –High sensitivity C Reactive Protein

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